"The Balch (6,983,763) method uses electroosmotic and/or electrophoretic force and turns "ON" electric current through a solution AFTER the solution has come into contact with the substrate. Thus, high polymers are made to mvoe by the effects of the current.

"Our invention is totally different from Balch in that the capillary and substrate are kep at all times apart from each other, thus, no electric current flows. Voltage is applied across the capillary and the substrate so that electric fields are produced. A solution electrified thusly is attracted toward the substrate from the bottom of the capillary. A "marginal" or very small amount of the solution is then made to swell out of the bottom and by the force of attraction, and dribble and be deposited onto the substrate. This method of deposition does not require the substrate to be wetted with the solutions, such as done by Balch. Also, no current need be turned on.

"In the invention , it is possible to deposit an extremely marginal amount of solution at the moment the solution comes into contact with the substrate,sine attractive force arises between the solution and the substrate before the contact occurs. Thus, the invention is based on a totally different principle than is applied by Balch, in which the electrophoretic force does not arise until the solution comes into contact with the substrate.

"Please note that although DNA is amplified within the capillary, this has nothing to do with depositing of the solution onto the substrate.

"Also, for the Examiner's edification, PCR can be speeded up by using thinner capillaries. According to our invention, it is

possible to reduce the operating time and prevent contamination with dust, by using both PCR and thin capillaries for spotting DNA solution at the same time.

"The foregoing advantages are nowwhere found in the prior art, and surely not in Balch or Haff."

In view of the foregoing, allowance is respectfully solicited.

respectfully

M. KOJIMA

MOONRAY KOJIMA
BOX 627
WWILLIAMSTOWN, MA 01267
Tel (413)458-2880
22 April 02

WHAT IS CLAIMED IS:

36. A method of producing biochips comprising the steps of:

arranging a plurality of capillaries having bottom open ends disposed at predetermined spacing so that said open ends are adjacent to and above a planar substrate, said open ends having diameters which prevent biomolecules from dropping down by force of gravity under non-depositing condition;

providing said biomolecules in said plurality of capillaries;

providing polymerase chain reaction to amplify said biomolecules within said plurality of capillaries;

applying a voltage across said plurality of capillaries and said substrate during a depositing condition to allow said biomolecules to move downward by force of [gravity] attraction through said open ends to deposit said biomolecules on sites on said substrate at space intervals coinciding with said predetermined spacing of said plurality of capillaries; and

stopping applying of said voltage during said non-depositing condition so that said biomolecules are held within said plurality of capillaries by surface tension at said open ends which is greater than said gravity; whereby

accurate efficient control of said voltage applying causes uniform and reliable deposits of said biomolecules on said substrate.

37. The method of claim 36, wherein said polymerase chain reaction is performed by atmospheric temperature change or by heating with laser irradiation.

APPENDIX "A"

MARKED UP COPY

38. An apparatus for producing biochips comprising:

a plurality of capillaries having bottom open ends arranged at a same spacing interval as that of sites on a planar substrate disposed below said open ends of said plurality of capillaries, said open ends having diameters which prevent biomolecules contained within said plurality of capillaries from falling down by force of gravity under normal non-depositing state;

amplifying means for providing polymerase chain reaction to amplify said biomolecules within said plurality of capillaries;

adjusting means for adjusting a gap formed between said open ends of said plurality of capillaries and said planar substrate by moving either said plurality of capillaries or said planar substrate, or both;

transfer means for transferring said biomolecules from said plurality of capillaries to said sites on said planar substrate during said depositing state, and for enabling said biomolecules to remain in said plurality of capillaries during said non-depositing state, said transfer means comprising:

voltage means for applying voltage across said plurality of capillaries and said planar substrate so that biomolecules contained in said plurality of capillaries and usually held therein by surface tension at said open ends are deposited by force of {gravity} attraction onto said sites of said planar substrate; and

stopping means for stopping applying voltage so that said surface tension of said open ends causes said biomolecules

MARKED UP COPY

to be held within said plurality of capillaries during said non-depositing state against force of gravity;

whereby accurate control of said transfer means produces reliable and uniform biomolecule chips.

39. The apparatus of claim 38, wherein said amplifying means comprises means for providing said polymerase chain reaction by temperature processing.

Add claims 40, 41 appearing in clean copy as "New Appendix 'D'"

APPENDIX "C"

MARKED UP COPY